REMARKS

Claims 1-44 were presented at the time of entry into the national phase under 35 USC 371. By preliminary amendment accompanying the filing, claims 1-44 were canceled and new claims 45-63 were entered. In response to a Restriction Requirement, claims 45-62 were elected; claim 63 is withdrawn from consideration. In response to an election of species for examination, Applicants elected the species of claim 46 in which R is hydrogen for the treatment of bacterial infection. This species is read upon by claims 45-48; 54-56 and 58-62. In the current communication, claim 45 is amended; no new matter has been added with this amendment. One portion of the amendment of claim 45 involves the addition of "a saccharide moiety" as a choice for R. Support for this amendment can be found in the published PCT application (WO 2004/064715) from which this application claims priority: page 14, lines 5 and 12-17; page 16, line 4 to page 17, line 6; and page 39, example 9.

It is believed that the Examiner's rejections are overcome with the following arguments, so no additional claims are currently cancelled or withdrawn. Therefore, the claims currently pending are 45-62.

Rejection of claims under 35 U.S.C § 112

Claims 45-48 and 54-62 are rejected under section 112, second paragraph as being indefinite. Claim 45 has been amended to further clarify the claimed invention:

> "1. A method of immunomodulation in the treatment or prophylaxis of conditions in which stimulation, augmentation or induction of the immune system is indicated and/or in which suppression or elimination of part or all of the immune response is indicated comprising administering to a patient in need of such treatment a therapeutically effective amount of a polyhydroxylated pyrrolizidine compound of formula..."

Support for this amendment can be found in the first paragraph on page 23 of the published PCT application (WO 2004/064715) from which this application claims priority:

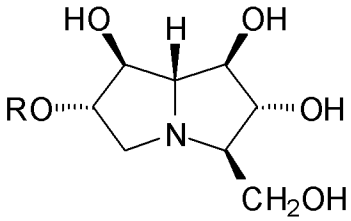
> "The pyrrolizidine compounds of the invention are immunomodulators. Thus, they find general application in the treatment or prophylaxis of conditions in which stimulation, augmentation or induction of the immune system is indicated and/or in which suppression or elimination of part or all of the immune response is indicated."

Applicant respectfully asserts that this amendment overcomes the § 112 rejection.

Rejection of claims under 35 U.S.C § 103(a)

Claims 45-48 and 54-62 are rejected under 35 U.S.C § 103(a) over Asano, et al., in view of Immune-strategy. Applicants believe this rejection is improper because the Examiner has not established a *prima facie* case for obviousness.

Asano: The elected compound of the instant application (wherein R is hydrogen) is shown below:



Asano does not disclose this compound, as the Examiner states. In Asano, none of compounds A_1, A_2, A_3, B_3, B_1, B_2 have an OH group at the 6-position; only C_1 shows an OH at this position. However, compound C_1 has an additional group (methyl) at the 5-position, as do four of the other six disclosed Asano compounds. The compound of applicants' elected species does not contain this additional methyl group at this position. The stereochemistry of the elected compound, moreover, is different from that of either Asano compound (B_3 and C_1) having a C-7 hydroxyl. Lastly, no data or utility is disclosed for compound C_1, and compound B_3 (arguably the next closest compound to the elected species) shows the poorest inhibition of bacterial glucosidase of any of the tested compounds in the IC_{50} results given in Table 2. Thus, to get from Asano's compounds to the compound of Applicants' elected species, the person of skill would have to (1)

choose the least potent species from Asano as the starting point [see Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd., 492 F.3d 1350, 83 U.S.P.Q.2d 1169 (Fed. Cir. 2007). "[T]he prior art disclosed a broad selection of compounds any one of which could have been selected as a lead compound for further investigation. Significantly, the closest prior art compound (compound b, the 6-methyl) exhibited negative properties that would have directed one of ordinary skill in the art away from that compound."]; (2) remove a carbon substituent at C-5; (3) invert a hydroxyl at C-1; (4) invert a hydroxyl at C-7 and (5) invert a hydroxyl at C-6. The examiner has provided no teaching that would motivate any of these changes. Whether or not Asano had taught the utility of his species as antibacterials (which he did not), a *prima facie* case of obviousness against the elected species could not exist.

Immune-strategy: The Examiner contends that, "Immune-strategy teaches glycosidase inhibitor in combination with ZDV for the treatment of HIV. Treatment of HIV encompasses treatment of bacterial infections that result from the disease" (page 4, section 7 of Action). Applicants respectfully disagree that this reference is relevant to the claims of the instant application. Immune-strategy describes plans for using a combination therapy of a known antiretroviral (ZDV) and a glycosidase inhibitor for the treatment of HIV, a virus.

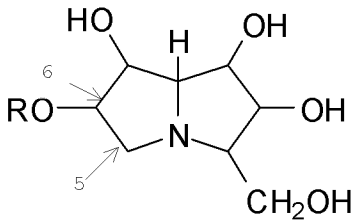
Any bacterial infection present in an HIV patient is merely a sequela of the viral infection, not the cause of it. The combination of ZDV and a glycosidase inhibitor will treat solely the viral cause, not the resulting bacterial infection. The combination of ZDV and a glycosidase inhibitor is not a known treatment for bacterial infection. Further, this is a combination therapy; there is absolutely no teaching that the glycosidase inhibitor by itself has any antibacterial activity whatsoever.

In the Immune-strategy reference, there is no action of a glycosidase inhibitor directly on bacterial cell walls. Indeed, there ARE no bacteria to act on, if the combination antiviral treatment has been effective. The prevention of the viral disease (HIV) prevents the occurrence of subsequent bacterial infection development. Claim 48 of the instant application specifically mentions the modification of bacterial cell walls ("A method according to claim 45 wherein the pyrrolizidine compound, when administered *in vivo*, modifies…bacterial cell walls"). This is

clearly not the intention of the treatment in the Immune-strategy reference.

The person of skill would not have had any suggestion or motivation to combine Asano with Immune-strategy to arrive at the instant claims: Asano does not even disclose the instant species, and Immune-strategy discloses a treatment to a viral infection, not a modification of the bacterial wall. This would not have been obvious to try. The person of ordinary skill would not have had reason to attempt to combine these two references, nor would there have been a reasonable expectation of success. Applicants argue that this combination of references decidedly does not constitute a *prima facie* obviousness rejection. Withdrawal of this rejection is respectfully requested.

Since the rejection of the species is not supportable, the Examiner is now required to continue examination of the remainder of the pending claims. Even when the entire claim set is considered, the above arguments overcoming Asano remain compelling. The broadest formula contained in the instant application is shown below:



Just as was found in the case of the elected species, this broader compound formula is not obvious in light of Asano. Asano clearly does not disclose the genus claimed nor any species within that genus. As discussed in the above arguments, the 5-position of Asano's Hyacinthacine C_1 contains a methyl group and doesn't disclose a utility. Those Asano compounds that have hydrogen at the 5-position (e.g. A_2) don't have the -OR group at the 6-position. Further, as mentioned above, the person of skill would still have to choose Asano's least potent species as the starting point, then change the structure by adding an -OR group and removing a methyl substituent. The *prima facie* obviousness rejection still cannot be made against the broad claims on the basis of the structures in the cited art.

Claim Objections

Because it is believed that the rejections are overcome, Applicants are not acquiescing to the withdrawal or cancellation of any of claims 45-48 and 54-62 at this time.

The Commissioner is hereby authorized to charge payment of the three-month extension of time fees that are due and any additional fees that may be required, or credit any overpayment of same, to Deposit Account No. 08-1935, Reference No. 3073.054.

Respectfully submitted,

Kellie S. Fredericks
Agent for Applicant
Reg. No. 61,998

Dated: June 23, 2009

HESLIN ROTHENBERG FARLEY & MESITI P.C.
5 Columbia Circle
Albany, New York 12203
Telephone: (518) 452-5600
Facsimile: (518) 452-5579